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TRANSMITTAL LETTER TO THE UNITED STATES DESIGNATED/ELECTED OFFICE (DO/EO/US) CONCERNING A FILING UNDER 35 U.S.C. 371

ATTORNEY DOCKET NUMBER: 3399-4006

U.S. APPLICATION NO. (If known, see 37 CFR 1.5): 10/030902

INTERNATIONAL APPLICATION NO.	INTERNATIONAL FILING DATE	EARLIEST PRIORITY DATE CLAIMED
PCT/GB00/02616	07 July 00 (07.07.00)	09 July 99 (09.07.99)

TITLE OF INVENTION: IMPROVEMENTS IN AND RELATING TO DELIVERY CAPSULES

APPLICANT(S) FOR DO/EO/US: Edward NOWAK, Barry John MUNCASTER and Malcolm David BROWN

Applicant herewith submits to the United States Designated/Elected Office (DO/EO/US) the following items and other information:

1. ☒ This is a **FIRST** submission of items concerning a filing under 35 U.S.C. 371.
2. ☐ This is a **SECOND** or **SUBSEQUENT** submission of items concerning a filing under 35 U.S.C. 371.
3. ☒ This is an express request to begin national examination procedures (35 U.S.C. 371(f)). The submission must include items (5), (6), (9) and 21 indicated below.
4. ☒ The US has been elected by the expiration of 19 months from the priority date (Article 31).
5. ☒ A copy of the International Application as filed (35 U.S.C. 371(c)(2))
   a. ☐ is attached hereto (required only if not communicated by the International Bureau).
   b. ☒ has been communicated by the International Bureau.
   c. ☐ is not required, as the application was filed in the United States Receiving Office (RO/US).
6. ☐ An English language translation of the International application as filed (35 U.S.C. 371(c)(2)).
   a. ☐ is attached hereto.
   b. ☐ has been previously submitted under 35 U.S.C. 154(d)(4).
7. ☒ Amendments to the claims of the International Application under PCT Article 19 (35 U.S.C. 371(c)(3))
   a. ☒ are attached hereto (required only if not communicated by the International Bureau).
   b. ☒ have been communicated by the International Bureau.
   c. ☐ have not been made; however, the time limit for making such amendments has NOT expired.
   d. ☐ have not been made and will not be made.
8. ☐ An English language translation of the amendments to the claims under PCT Article 19 (35 U.S.C. 371(c)(3)).
9. ☒ An oath or declaration of the inventor(s) (35 U.S.C. 371(c)(4)).
10. ☐ An English language translation of the annexes to the International Preliminary Examination Report under PCT Article 36 (35 U.S.C. 371(c)(5)).

Items 11. to 16. below concern document(s) or information included:

11. ☒ An Information Disclosure Statement under 37 CFR 1.97 and 1.98 with PTO 1449 and copy of all cited references.
12. ☐ An assignment document for recording. A separate cover sheet in compliance with 37 CFR 3.28 and 3.31 is included.
13. ☒ A FIRST preliminary amendment.
14. ☐ A SECOND or SUBSEQUENT preliminary amendment.
15. ☐ A substitute specification.
16. ☐ A change of power of attorney and/or address letter.
17. ☐ A computer-readable form of the sequence listing in accordance with PCT Rule 13ter.2 and 35 U.S.C. 154(d)(2) with copy of Statement Under 37 CFR Section 1.821(f) and WIPO Standard ST.25 as filed with the International Bureau of WIPO.
18. ☐ A second copy of the published international application under 35 U.S.C. 154(d)(4).
19. ☐ A second copy of the English language translation of the international application under 35 U.S.C. 154(d)(4).

APPLICATION NO. (if known, see 37 C.F.R. 1.51)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NO.
TBA	PCT/GB00/02616	3399-4006

20. ☒ Other items or information:

Copies of:

Published PCT/GB00/02616, International Publication Number WO 01/03676 (with International Search Report);

Demand (Form PCT/IPEA/401);

Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416);

International Preliminary Examination Report (Form PCT/IPEA/409);

Notice Informing the Applicant of the Communication of the International Application to the Designated Offices (Form PCT/IB/308);

Notification Concerning Submission or Transmittal of Priority Document (Form PCT/IB/304);

Information Concerning Elected Offices Notified of Their Election (Form PCT/IB/332); and

Request (4 pages).

U.S. APPLICATION NO. (if known, see 37 C.F.R. 1.51)	INTERNATIONAL APPLICATION NO.	ATTORNEY'S DOCKET NUMBER
10/030902 (IB)	PCT/GB00/02616	3399-4006

21. ☒ The following fees are submitted:

BASIC NATIONAL FEE (37 CFR 1.492 (a) (1) - (5)):

Neither international preliminary examination fee (37 CFR 1.482) nor international search fee (37 CFR 1.445(a)(2) paid to USPTO and International Search Report not prepared by the EPO or JPO $1040.00

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but International Search Report prepared by the EPO or JPO $890.00

International preliminary examination fee (37 CFR 1.482) not paid to USPTO but international search fee (37 CFR 1.445(a)(2) paid to USPTO ... $740.00

International preliminary examination fee paid to USPTO (37 CFR 1.482) but all claims did not satisfy provisions of PCT Article 33 (1) - (4) $710.00

International preliminary examination fee paid to USPTO (37 CFR 1.482) and all claims satisfied provisions of PCT Article 33(1) - (4) $100.00

	CALCULATIONS	PTO USE ONLY
ENTER APPROPRIATE BASIC FEE AMOUNT =	$ 890.00	
Surcharge of **$130** for furnishing the oath or declaration later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(e)).		

CLAIMS	NUMBER FILED	NUMBER EXTRA	RATE		
Total claims	47 - 20 =	27	X $18.00	$ 486.00	
Independent claims	3 - 3 =	0	X $84.00	$ -0-	
MULTIPLE DEPENDENT CLAIM(S) (if applicable)			+ $280.00	$ 280.00	
TOTAL OF ABOVE CALCULATIONS =				$1,656.00	
☒ Applicant claims small entity status. See 37 C.F.R. 1.27. The fees indicated above are reduced by 1/2.				$ 828.00	
SUBTOTAL =				$ 828.00	
Processing fee of **$130.00** for furnishing the English translation later than ☐ 20 ☐ 30 months from the earliest claimed priority date (37 CFR 1.492(f)).				$	
TOTAL NATIONAL FEE =				$ 828.00	
Fee for recording the enclosed assignment (37 CFR 1.21(h)). The assignment must be accompanied by an appropriate cover sheet (37 CFR 3.28, 3.31). **$40.00** per property X =				$	
TOTAL FEES ENCLOSED =				$ 828.00	
				Amount to be refunded:	$
				charged:	$

a. ☐ A check in the amount of $ to cover the above fees is enclosed.

b. ☒ Please charge my Deposit Account No. 13-4500, ORDER NO. **3399-4006** in the amount of **$828.00** to cover the above fees.

c. ☒ The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account No. 13-4500, ORDER NO. 3399-4006. **A duplicate copy of this sheet is enclosed.**

d. ☐ Fees are to be charged to a credit card. **WARNING:** Information on this form may become public. **Credit card information should not be included on this form.** Provide credit card information and authorization on PTO-2038.

NOTE: Where an appropriate time limit under 37 CFR 1.494 or 1.495 has not been met, a petition to revive (37 CFR 1.137(a) or (b)) must be filed and granted to restore the application to pending status.

SEND ALL CORRESPONDENCE TO:

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Docket No. 3399-4006

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant(s)	:	Edward NOWAK, Barry John MUNCASTER, and Malcolm David BROWN		
International Application No:		PCT/GB00/02616		
Serial No.	:	TBA	Group Art Unit :	TBA
Filed	:	January 9, 2002	Examiner :	TBA
For	:	IMPROVEMENTS IN AND RELATING TO DELIVERY CAPSULES		

Commissioner for Patents
Washington, D.C. 20231

PRELIMINARY AMENDMENT

Dear Sir:

Please enter the following Preliminary Amendment prior to consideration of the application on the merits.

IN THE CLAIMS

Please cancel claims 1-14 as set forth in the Article 19 amendment to the above-identified application, and substitute therefor the following new claims:

15. (new) A delivery capsule having at least two separate chambers, the capsule including a dividing wall or septum defining in part two separate chambers, wherein the dividing wall or septum comprises two layers of material adhered together.

16. (new) A capsule according to claim 15, wherein each chamber contains a different material.

17. (new) A capsule according to claim 15, wherein each chamber contains a metered dose of a material.

18. (new) A capsule according to claim 16, wherein each chamber contains a metered dose of a material

19. (new) A capsule according to claim 15, wherein the dividing wall or septum comprises a median wall symmetrically arranged to form two chambers of similar size and shape.

20. (new) A capsule according to claim 16, wherein the dividing wall or septum comprises a median wall symmetrically arranged to form two chambers of similar size and shape.

21. (new) A capsule according to claim 17, wherein the dividing wall or septum comprises a median wall symmetrically arranged to form two chambers of similar size and shape.

22. (new) A capsule according to claim 15, formed from a heat-sealable material that is capable of deforming plastically on heating and/or when partially solvated.

23. (new) A capsule according to claim 16, formed from a heat-sealable material that is capable of deforming plastically on heating and/or when partially solvated

24. (new) A capsule according to claim 17, formed from a heat-sealable material that is capable of deforming plastically on heating and/or when partially solvated

25. (new) A capsule according to claim 19, formed from a heat-sealable material that is capable of deforming plastically on heating and/or when partially solvated

26. (new) A capsule according to claim 22, wherein the capsule is formed from one or more materials selected from the group consisting of: hydroxy propyl methyl cellulose, pectin, polyethylene oxide, polyvinyl alcohol, alginate, polycaprolactone, and gelatinised starch based materials.

27. (new) A capsule according to claim 26, wherein at least part of the capsule material carries a coating.

28. (new) A capsule according to claim 15, wherein said at least two chambers are designed to release their contents under similar circumstances.

29. (new) A capsule according to claim 16, wherein said at least two chambers are designed to release their contents under similar circumstances.

30. (new) A capsule according to claim 17, wherein said at least two chambers are designed to release their contents under similar circumstances.

31. (new) A capsule according to claim 19, wherein said at least two chambers are designed to release their contents under similar circumstances.

32. (new) A capsule according to claim 22, wherein said at least two chambers are designed to release their contents under similar circumstances.

33. (new) A capsule according to claim 26, wherein said at least two chambers are designed to release their contents under similar circumstances.

34. (new) A capsule according to claim 27, wherein said at least two chambers are designed to release their contents under similar circumstances.

35. (new) A capsule according to claim 15, wherein said at least two chambers are designed to release their contents under different circumstances.

36. (new) A capsule according to claim 16, wherein said at least two chambers are designed to release their contents under different circumstances.

37. (new) A capsule according to claim 17, wherein said at least two chambers are designed to release their contents under different circumstances.

38. (new) A capsule according to claim 19, wherein said at least two chambers are designed to release their contents under different circumstances.

39. (new) A capsule according to claim 22, wherein said at least two chambers are designed to release their contents under different circumstances.

40. (new) A capsule according to claim 26, wherein said at least two chambers are designed to release their contents under different circumstances.

41. (new) A capsule according to claim 27, wherein said at least two chambers are designed to release their contents under different circumstances.

42. (new) A capsule according to claim 28, wherein said at least two chambers are designed to release their contents under different circumstances.

43. (new) A capsule according to claim 35, wherein different chambers of the capsule are defined at least in part by different materials.

44. (new) A capsule according to any one of claims 15, 16, 17, 19, 22, 26, 27, 28, or 35, wherein the capsule is formed at least in part from hydroxy propyl methyl cellulose.

45. (new) A capsule according to claim 44, wherein at least part of the hydroxy propyl methyl cellulose is coated with alginate.

46. (new) A method of encapsulation comprising supplying two films of material capable of deforming plastically on heating and/or when partially solvated; heating the films and/or applying solvent; forming the films into suitably shaped capsule portions; supplying respective substances to be encapsulated to capsule portions of each film; supplying a respective film of a dividing septum material to each of the filled capsule portions; and sealing the capsule portions and septum material together to form a capsule having at least two separate chambers.

47. (new) Encapsulation apparatus comprising means for supplying two films of material to an encapsulation unit; means for plastically deforming each film to form suitably shaped capsule portions; means for supplying respective substances to be encapsulated to the respective capsule portions of each film; means for supplying a respective film of dividing septum material to each of the filled capsule portions; and means for sealing together the capsule portions and septum material to produce a capsule having at least two separate chambers. --

REMARKS

The application contains multiple dependent claims improperly dependent from multiple dependent claims. To correct this defect, claims 3, 4-5, 8-9 and 11 have been amended, and new claims added. All claims have been consecutively renumbered. No new matter is introduced. This amendment is not made for reasons related to the patentability of the claimed subject matter, but is made solely to remove improperly multiple dependent claims.

Respectfully submitted,

Dated: January 9, 2002

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Title: Improvements in and relating to Delivery Capsules

Field of the Invention

This invention relates to a delivery capsule, that is, a capsule designed to retain and protect its contents until an intended site of delivery or conditions of delivery are encountered, at which point the capsule contents are released.

Background to the Invention

Delivery capsules are well known and find particular application in the form of ingestible gelatin capsules for the delivery of accurately metered doses of pharmaceutical preparations and dietary supplements. Liquid preparations are typically encapsulated in soft gelatin capsules and particulate or powdered preparations are typically encapsulated in two part hard gelatin capsules. The capsules are designed to release their contents after ingestion, typically by solution of the capsule wall, and by use of suitable capsule material can thus provide a means of administering a dose of a preparation at a desired appropriate site in the body. The finished capsules offer protection to the contents yet solubility within the body.

Other uses of delivery capsules include delivery of cosmetic ingredients, eg fragranced bath oils encapsulated in soft gelatin capsules for release into bath water, paint balls in the form of paint-containing capsules that rupture on impact etc.

There are limitations on current capsules and encapsulation techniques. For example, because of differences in powder and liquid handling, the processing means for the encapsulation of powders and liquids within a gelatin capsule are quite distinct and incompatible. This situation renders impossible the provision of a gelatin capsule containing both powder and liquid that are kept separate.

The present invention seeks to address certain shortcomings and limitations of current capsules and encapsulation techniques.

Summary of the Invention

In one aspect the invention provides a delivery capsule having at least two separate chambers.

The chambers of the capsule are completely discrete and separated from each other so that no communication between the chambers is possible. This means that the contents of the different chambers are kept separate from each other within the capsule until delivery.

In most cases, different chambers of the capsule will contain different materials, possibly in different physical forms, eg liquid, solid (eg tablet, particulate, powdered), slurry etc, in a way that has not hitherto been possible, although it is also possible for the different chambers to contain separate doses of the same material.

The capsule is preferably internally divided by a dividing wall or septum, conveniently in the form of a median wall symmetrically arranged to form two chambers of similar size and shape.

One or more chambers of the capsule may be further divided if required, eg by inclusion in a chamber of a smaller delivery capsule, constituting a further separate chamber.

The invention thus provides a compartmented capsule in a way that has not been done hitherto. Indeed, it is believed that this is not possible with known techniques for gelatin encapsulation.

Instead of using gelatin for encapsulation, the present invention preferably uses a heat-sealable material that is capable of deforming plastically on heating (a thermoplastic material) and/or that is capable of deforming plastically when partially solvated by

application of an appropriate solvent. Suitable materials include hydroxy propyl methyl cellulose (HPMC), pectin, polyethylene oxide, polyvinyl alcohol, alginate, polycaprolactone, gelatinised starch-based materials etc. The material may be coated, eg with gum arabic, pectin, alginate eg sodium alginate etc to modify properties. For example, gum arabic, pectin and alginate all have a slight retarding effect on HPMC solubility, the extent of the effect varying according to coating thickness. Further, both pectin and alginate can be cross-linked, eg with calcium, this has the effect of making the material pH sensitive such that it will not dissolve in the mouth but will dissolve in the stomach where pH is lower. Multi-layer materials may also be used. Examples of suitable capsule materials and coatings are given in WO 97/35537 and WO 00/27367. The capsule materials also have the advantage compared with gelatin of being non-animal derived, and so having no possibility of transmitting animal-related diseases such as bovine spongiform encepehalopathy (BSE). Such materials are commercially available, eg in the form of ribbon-like films or can be readily manufactured, eg by extrusion from solution. One currently favoured material is the thermoplastic material HPMC, in expanded or non-expanded form, with or without coatings. HPMC is suitable for ingestion by humans and so can be used for ingestible capsules as well as other uses, eg culinary, cosmetic etc.

A compartmented capsule in accordance with the invention can be used simply to keep separate in the respective chambers two materials prior to delivery. This can be of advantage, for example, when delivering to the same site two materials which react together on admixture: by use of a compartmented capsule in accordance with the invention the two materials can be kept separate until the septum wall is dissolved on delivery, bringing the materials together. This approach is also useful, say, for delivery of two separate pharmaceutical preparations. For instance, this approach is relevant to delivery of certain multi-component cold remedies which are currently unable to get FDA approval due to concerns of possible chemical reactions prior to ingestion: by using a capsule in accordance with the invention to keep the components separate within the capsule prior to delivery such difficulties can be overcome. As a further example, there is a drug called Acctuane which is an effective treatment for acne but which can also cause birth defects. In order to ensure that this does not occur birth control drugs should be

taken simultaneously with Acctuane by fertile female users. For safety reasons it would thus be far preferable if the birth control drug and the acne remedy were taken together, but kept separate until after ingestion. This can be readily achieved by use of a compartmented capsule in accordance with the invention.

Furthermore, by using different materials (either in terms of thickness and/or composition and/or coatings) defining the different chambers of the capsule, it is possible to arrange for release of the contents of the different chambers under different conditions, eg at different specific sites within the body. The contents of different compartments can thus be targeted to different specific areas within the body.

For instance, use of a thicker material defining one compartment may result in slightly delayed release of material compared with that from a compartment defined by a thinner layer of similar material.

Another example is the use of a pH sensitive coating on the material defining one chamber so that chamber contents are released at different delivery sites dependent upon pH. Use of enteric coatings such as cellulose acetate phthalate can also be used to target release, eg to within the stomach. Coatings such as ethyl cellulose can be used to retard solubility times. A further example is use of expanded HPMC defining one compartment and non-expanded HPMC defining another compartment. Expanded HPMC film releases rapidly in the mouth while standard, non-expanded film has sufficient resistance to dissolution to release only after it has been swallowed, providing that it is not kept in the mouth too long.

It is also possible to coat a finished capsule after formation with materials such as sodium alginate to improve robustness or alter solubility.

The capsule materials may include optional colourings, eg in the form of known food dyes such as FD and C yellow number 5, optional flavourings, textures etc.

The capsules may have a range of different sizes and shapes as appropriate dependent on intended usage. Capsules are typically generally spherical, ovoid, cylindrical etc in shape, preferably incorporating a median septum as described above. Typical maximum dimensions of the capsule are in the range 3mm to 20mm, but other sizes are possible.

The capsules are conveniently made by a vacuum or pressure forming technique, that may be loosely based on the technique described in WO 97/35537 but with very substantial modification.

In a further aspect, the invention thus provides a method of encapsulation, comprising supplying two films of material capable of deforming plastically on heating and/or when partially solvated; heating the films and/or applying solvent; forming the films into suitably shaped capsule portions; supplying respective substances to be encapsulated to capsule portions of each film; supplying a film of a dividing septum material to at least one of the filled capsule portions; sealing the capsule portions and septum material together to form a capsule having at least two separate chambers.

The films are preferably formed into capsule portions by application of elevated pressure or vacuum (or reduced pressure).

It is preferred to use two layers of film for producing the septum, with one film applied to each respective capsule portion, as handling including optional coating is easier.

Adhesive material is preferably applied to the various film materials to help secure the capsule portions and septum together. Capsule sealing is preferably accomplished by heat sealing, to fuse the films of material together, although other sealing methods may be used.

Pre-formed films of material may be used. Alternatively, the films may be formed during the encapsulating process, eg by being cast from solution.

In a further aspect the invention provides encapsulation apparatus, comprising means for supplying two films of material to an encapsulation unit; means for plastically deforming each film to form suitably shaped capsule portions; means for supplying respective substances to be encapsulated to the respective capsule portions of each film; means for supplying a film of dividing septum material to at least one of the filled capsule portions; and means for sealing together the capsule portions and septum material to produce a capsule having at least two separate chambers.

The apparatus typically also comprises reservoirs of the substances to be encapsulated, with associated supply arrangements adapted to supply a metered doses of the substance to the capsule portions at predetermined time intervals. The arrangement may employ syringe pumps or the like.

The apparatus conveniently includes heater means for heating the capsule film material to enable thermoplastic deformation.

The means for deforming the films conveniently comprises a pair of similar vacuum belts.

The invention is applicable to encapsulation of a wide range of pharmaceutical, culinary, cosmetic etc ingredients, enabling delivery to different sites of different materials or delivery to the same site of materials that are desirably kept separate prior to delivery.

Capsules described in this specification provide a delivery means with either at least two distinct liquid or solid, eg powder fills, or a combination of liquid and solids, eg powder. The materials can also be selected so as to exclude gelatin. The combination of materials used for the capsule wall and capsule dividing septum can be chosen to release either or both parts of the contents of capsule at specific sites within the body. These components can then address two different specific areas or act synergistically when mixed on release at the same site. In the latter example the capsule is serving to prevent the mixing of the two components prior to them reaching the correct site within the body as well as providing an accurate dose and blend of components for maximum efficacy.

The present invention enables the encapsulation of both powders and liquids within discrete chambers in an ingestible capsule. Using pre-formed rolls of film such as hydroxy propyl methyl cellulose capsules are formed with an outer shell and a dividing septum. In such a capsule two different materials which would react if brought together in a single chamber can be kept apart until the septum wall is dissolved.

By the application of surface coatings to the forming rolls and the dividing layer prior or post capsule formation, or the use of different materials for the forming rolls, capsules can be formed which release their contents under different environmental conditions. An example of this is the application to pH sensitive coatings on the outer surface of the capsule wall and septum which causes the two distinct chambers to release their contents at different delivery sites dependent upon the pH of the surrounds.

The capsules are produced on dedicated machinery employing the use of vacuum forming and heat sealing, and can be filled with liquids or powders.

The invention will be further described, by way of illustration, with reference to the accompanying drawings in which:

Figure 1 is a schematic sectional view of a delivery capsule in accordance with the invention; and

Figure 2 is a schematic representation of one embodiment of apparatus in accordance with the invention for producing a delivery capsule embodying the invention.

Detailed description of the Drawings

Referring to the drawings, Figure 1 illustrates schematically a generally ovoid delivery capsule 10 comprising at outer shell or wall in the form of two similar half shells 12 and 14 each of generally semi-ovoid form, and a median dividing wall of septum 16 that

divides the capsule into two similar chambers or compartments 18 and 20 that are completely separate from each other, with no communication between the chambers 18 and 20 being possible.

Each chamber 18 and 20 contains a metered amount of a different material (not shown), eg with a powdered or particulate material in chamber 18 and a liquid material in chamber 20, or visa versa, or with different liquid materials in each of the two chambers or with different powdered or particulate materials in each of the two chambers.

The half shells 12 and 14 of the septum 16 may be made of similar or different materials, depending on the desired properties and intended use of the capsule.

For example, where the function of the compartments is simply to keep two materials separate from each other until release at the same site of delivery, thus can be achieved by all of the capsule walls, half shells 12 and 14 and septum 16, being of the same material, eg HPMC (possibly coated as discussed above).

However, where the capsule is designed to delivery the contents of chamber 18 and chamber 20 at different sites or under different conditions, eg at different sites in the body after ingestion, it is appropriate for the capsule walls to be of different material, eg with half shell 12 of a first material and half shell 14 and septum 16 of a second, different material, with the two different materials functioning to release the contents of the associated compartment under different conditions, eg under different conditions of pH, or after different time intervals etc. For example, the first material may comprise pectin and the second material may comprise HPMC. As a further example, the first material may comprise un-coated HPMC and the second material may comprise a HPMC coated, eg with sodium alginate. Another possibility is for the first and second materials to have different coatings, eg of sodium alginate and gum arabic. A yet further possibility is for the first material to be expanded HPMC, with the second material being standard cast HPMC coated with sodium alginate.

It is also possible for septum 16 to be of completely insoluble material that will, eg, pass through the body unchanged.

The dimensions of capsule 10 may be varied to suit the intended purpose of the capsule, with the maximum dimension typically being in the range 3mm to 20mm.

Examples

The following examples serve to give specific illustrations of this invention but they are not in any way intended to limit the scope of this invention.

Example 1. A dual delivery capsule as shown in Figure 1 where the septum 16, and the capsule walls 12 and 14 are of like material, exampled by hydroxy propyl methyl cellulose.

Example 2. A dual delivery capsule as shown in Figure 1 with one wall and dividing septum of like material, exampled by hydroxy propyl methyl cellulose, and the other wall of different material, exampled by pectin.

Example 3. A dual delivery capsule as shown in Figure 1 with walls and dividing septum of like material, exampled by hydroxy propyl methyl cellulose with a coating on one half of the capsule and one side of the capsule dividing septum, exampled by sodium alginate.

Example 4. A dual delivery capsule as shown in Figure 1 with walls and dividing septum of like material, exampled by hydroxy propyl methyl cellulose with the same coating on both sides of the capsule, exampled by sodium alginate.

Example 5. A dual delivery capsule as shown in Figure 1 with walls 12 and 14 of like material exampled by hydroxy propyl methyl cellulose with different coatings on each exampled by sodium alginate and gum arabic and dividing septum 16 coated on the side closest to the wall bearing the alginate coating with gum arabic.

Example 6. A dual delivery capsule as shown in Figure 1 with a liquid fill contained in chamber 20 exampled by dextromethorphan and a powder filled example by chlopheniramine contained in chamber 18 between septum 16 and capsule wall 12.

Example 7. A dual delivery capsule as shown in Figure 1 with two different liquid fills exampled by cod liver oil and evening primrose oil contained in chamber 20 and chamber 18, respectively.

Figure 2 illustrates schematically one embodiment of apparatus for producing capsules in accordance with the invention.

The illustrated encapsulation apparatus comprises two similar, aligned, side-by-side vacuum belts 40 and 42 each comprising a plurality of articulated segments of plastics-coated aluminium as represented by segment 44. Each segment has a width of about 600mm, extending perpendicular to the plane of the sectional view of Figure 2, and is formed with a row of hemi-ovoid recesses running across its width, eg recess 46, only one such recess of each segment being visible in the drawing. Drive means (not shown) are provided for driving the two belts synchronously, with belt 40 being driven in a clockwise direction and belt 42 being driven in an anticlockwise direction, with the recesses of the two belts in registration with each other. Each recess includes a number of fine bore vacuum ports (not shown), each about 0.4mm in diameter, with vacuum means (not shown) arranged to apply a vacuum in the range -15 to -30 inches mercury. The vacuum may be applied only to the recesses in the segments when in the upper portion of travel of the belts.

Four rolls of film material 50, 52, 54 and 56 are rotatably supported on respective spindles, with the films being pulled from the spindles and over vacuum belts by a driven nip roller 58. The films pass around respective guide rollers 60, 62, 64, 66 to be brought into contact with the associated vacuum belt.

Films 50 and 52 form the generally hemi-ovoid outer shell halves of a capsule. To this end, the films pass below respective infra red heaters 68 and 70 located near the outer end of each vacuum bed, which act to heat the film passing there below to a temperature at which it is capable of deforming plastically. The films then deform to take up the shape of the recesses in the vacuum belts, assisted by the vacuum applied to the belts.

The films, moving with the vacuum bed, then pass below respective adhesive application stations 72, 74 in the form of rollers which apply adhesive to the surface of the films not within the recesses.

The films then move past respective filling stations 76, 78 where metered doses of material are supplied to each outer shell half as it passes below the station. Suitable filling equipment for supplying metered doses of liquid materials (eg syringe pumps, peristaltic pumps etc) and for supplying metered doses of powdered or particulate materials are well known. Typical volume fills are in the range 0.1 to 3.0 mls per capsule half.

The filled outer shell halves then move inwardly with the vacuum bed, past guide rollers 64, 66 around which pass lengths of septum-forming films 54, 56. The septum-forming films adhere to the non-deformed parts of films 50 and 52 under the action of the previously applied adhesive, closing off the half capsules.

The thus formed half capsules move inwardly with the vacuum belt past further adhesive stations 80, 82 which act to apply adhesive to the top surface of the septum-forming films.

The capsule halves are brought together between adjacent sides of the vacuum belts and the two septums adhere together by adhesive action. At this point, the capsules are loosely stuck together.

The films with arrays of capsules therebetween are fed to a sealing station comprising two heater blocks 88, 90 mounted on pneumatic rams that reciprocate towards and away from each other in synchronism. The blocks act to heat and fully seal together the capsule

halves, forming compartmented capsules in accordance with the invention. A knife edge (not shown) is provided on one of the blocks to cut the capsules from the remaining material. The cut capsules are collected below and the remaining film web material is passed to waste.

In a typical embodiment the films comprise HPMC having a thickness of about 120nm. Such material is readily available commercially. For example, HPMC is available from Dow Chemicals (USA) and is made into a film by Cast Film Technologies (USA).

Optional coatings may be applied to the film material, eg upstream of the rollers. Different coatings may be applied to the different half-capsule forming films.

When treating HPMC, the films should be heated at heating stations to a temperature of about 85 to 90°C so as to become thermoplastic and deformable.

A suitable adhesive for use with HPMC is HPMC with 60% propylene glycol, which can be applied warm or cold. Other possible adhesive/plasticizer materials include triacetin, monoacetin and ethyl lactate.

The adhesive formulation can also be applied before the forming heaters provided that it is of food grade and there is no reaction with the capsule contents. In such a case there will be a continuous coating of the adhesive present inside the formed capsule half. This can help with adhesion of the septum-forming film by causing a build up inside the seam.

For sealing HPMC, the heating block should be heated to a temperature in the range 150 to 170°C.

When using PVA instead of HPMC, heater temperatures must be much higher, about 150°C to produce a thermoplastic film, with the heater block typically being heated to a temperature in the range 160 to 200°C.

The illustrated equipment can run at a rate capable of producing about 30,000 capsules per hour with a web width of about 600mm.

A typical embodiment uses expanded HPMC for one capsule half and standard cast HPMC coated with sodium alginate for the other capsule half. The standard cast HPMC has a thickness of about 120 micron with a coating of alginate in the range 2 to 10 microns thick.

The application of the first adhesive is conveniently effected by rolling, extrusion or spraying, preferably by use of a roller, while application of the second adhesive is conveniently effected by a roller in contact with the film.

The capsules produced by the apparatus of Figure 2 have a form generally corresponding to the capsule of Figure 1, with septum 16 being constituted by two adhered together layers of film 54 and 56. The capsules include a short peripheral median flange (not shown in Figure 1), aligned with and extending outwardly from the position of septum 16, constituted by portions of the four films 50, 52, 54, 56 adhered together to seal the compartments and capsule.

Claims

1. A delivery capsule having at least two separate chambers.

2. A capsule according to claim 1, wherein each chamber contains a different material.

3. A capsule according to claim 1 or 2, wherein each chamber contains a metered dose of a material.

4. A capsule according to claim 1, 2 or 3, including a dividing wall or septum defining in part two separate chambers.

5. A capsule according to claim 4, wherein the dividing wall or septum comprises two layers of material adhered together.

6. A capsule according to claim 4 or 5, wherein the dividing wall or septum comprises a median wall symmetrically arranged to form two chambers of similar size and shape.

7. A capsule according to any one of the preceding claims, formed from a heat-sealable material that is capable of deforming plastically on heating and/or when partially solvated.

8. A capsule according to claim 6, wherein the capsule is formed from one or more materials selected from hydroxy propyl methyl cellulose, pectin, polyethylene oxide, polyvinyl alcohol, alginate, polycaprolactone, gelatinised starch based materials.

9. A capsule according to claim 8, wherein at least part of the capsule material carries a coating.

10. A capsule according to any one of the preceding claims, wherein said at least two chambers are designed to release their contents under similar circumstances.

11. A capsule according to any one of claims 1 to 9, wherein said at least two chambers are designed to release their contents under different circumstances.

12. A capsule according to claim 11, wherein different chambers of the capsule are defined at least in part by different materials.

13. A capsule according to any one of the preceding claims, wherein the capsule is formed at least in part from hydroxy propyl methyl cellulose.

14. A capsule according to claim 13, wherein at least part of the hydroxy propyl methyl cellulose is coated with alginate.

15. A method of encapsulation comprising supplying two films of material capable of deforming plastically on heating and/or when partially solvated; heating the films and/or applying solvent; forming the films into suitably shaped capsule portions; supplying respective substances to be encapsulated to capsule portions of each film; supplying a film of a dividing septum material to at least one of the filled capsule portions; sealing the capsule portions and septum material together to form a capsule having at least two separate chambers.

16. Encapsulation apparatus comprising means for supplying two films of material to an encapsulation unit; means for plastically deforming each film to form suitably shaped capsule portions; means for supplying respective substances to be encapsulated to the respective capsule portions of each film; means for supplying a film of dividing septum material to at least one of the filled capsule portions; and means for sealing together the capsule portions and septum material to produce a capsule having at least two separate chambers.

Fig.1.

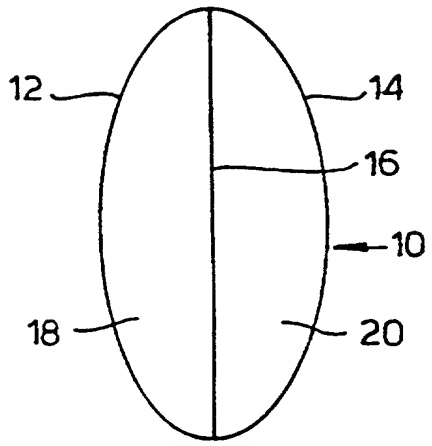
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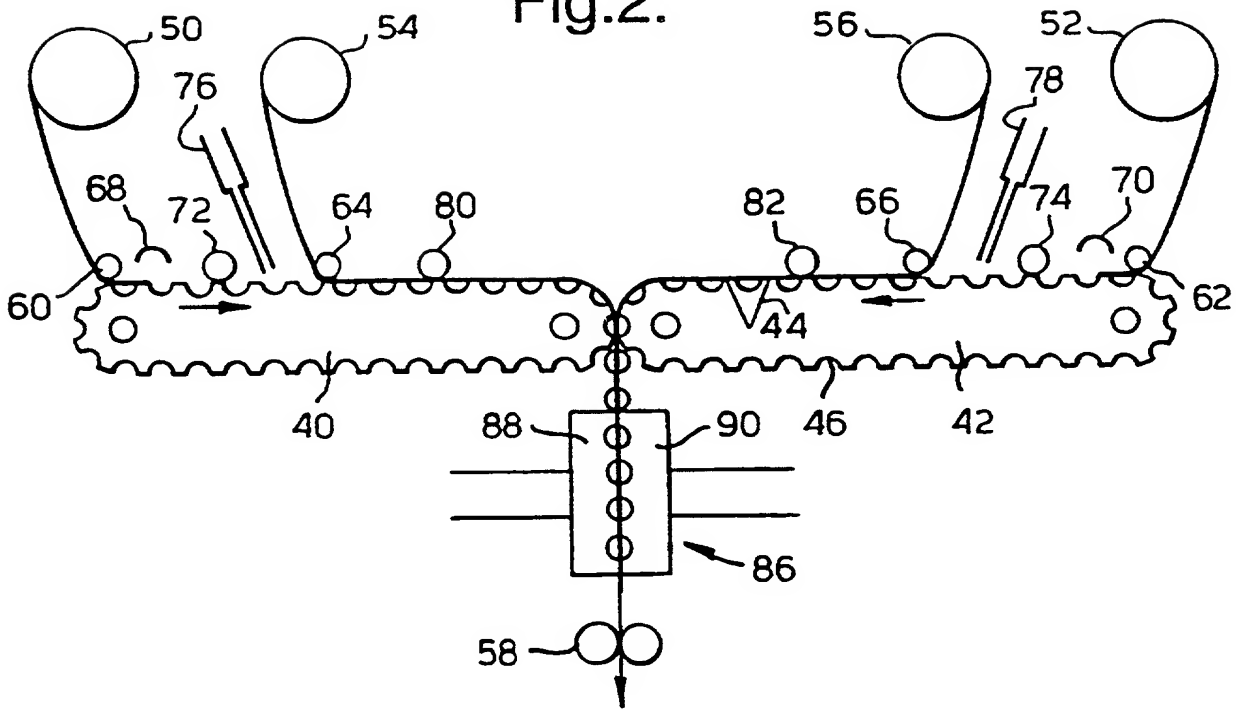
Fig.2.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☐ The attached 35 U.S.C. § 119 claim for priority for the application(s) listed below forms a part of this declaration.

Country/PCT	Application Number	Date of filing (day, month, yr)	Date of issue (day, month, yr)	Priority Claimed
GB	99160335	9 July 1999		☒ Y ☐ N
				☐ Y ☐ N
				☐ Y ☐ N

☐ I hereby claim the benefit under 35 U.S.C. § 119(e) of any U.S. provisional application(s) listed below.

Provisional Application No.	Date of filing (day, month, yr)

ADDITIONAL STATEMENTS FOR DIVISIONAL, CONTINUATION OR CONTINUATION-IN-PART OR PCT INTERNATIONAL APPLICATION(S DESIGNATING THE U.S.)

I hereby claim the benefit under Title 35, United States Code § 120 of any United States application(s) or under § 365(c) of any PCT international application(s) designating the U.S. listed below.

US/PCT Application Serial No.	Filing Date	Status (patented, pending, abandoned)/ U.S. application no. assigned (For PCT)
US/PCT Application Serial No.	Filing Date	Status (patented, pending, abandoned)/ U.S. application no. assigned (For PCT)

☐ In this continuation-in-part application, insofar as the subject matter of any of the claims of this application is not disclosed in the above listed prior United States or PCT international application(s) in the manner provided by the first paragraph of Title 35, United States Code, § 112, I acknowledge the duty to disclose material information as defined in Title 37, Code of Federal Regulations, § 1.56(a) which occurred between the filing date of the prior application(s) and the national or PCT international filing date of this application.

I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

I hereby appoint the following attorneys and/or agents with full power of substitution and revocation, to prosecute this application, to receive the patent, and to transact all business in the Patent and Trademark Office connected therewith: John C. Vassil (Reg. No. 19,098), Alfred P. Ewert (Reg. No. 19,887), David H. Pfeffer (Reg. No. 19,825), Harry C. Marcus (Reg. No. 22,390), Robert E. Paulson (Reg. No. 21,046), Stephen R. Smith (Reg. No. 22,615), Kurt E. Richter (Reg. No. 24,052), J. Robert Dailey (Reg. No. 27,434), Eugene Moroz (Reg.

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☒ I hereby authorize the U.S. attorneys and/or agents named hereinabove to accept and follow instructions from Keith W. Nash & Co. as to any action to be taken in the U.S. Patent and Trademark Office regarding this application without direct communication between the U.S. attorneys and/or agents and me. In the event of a change in the person(s) from whom instructions may be taken I will so notify the U.S. attorneys and/or agents named hereinabove.

1 - 00

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Inventor's signature* E. Nowak 7th January 2002 Date

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2 - 00

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Inventor's signature* B Muncaster 9th January 2002 Date

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Citizenship: Great Britain

Post Office Address: 8 Burling Walk, Milton, Cambridge CD4 6DX

3 - 00

Full name of third inventor: BROWN, Malcolm David

Inventor's signature* M Brown 8th January 2002 Date

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Citizenship: Great Britain

Post Office Address: 87 The Lammas, Mundford, Norfolk IP26 5DS

*Before signing this declaration, each person signing must:

1. Review the declaration and verify the correctness of all information therein; and

2. Review the specification and the claims, including any amendments made to the claims.

After the declaration is signed, the specification and claims are not to be altered.

To the inventor(s):

The following are cited in or pertinent to the declaration attached to the accompanying application:

Title 37, Code of Federal Regulation, §1.56

Duty to disclose information material to patentability

(a) A patent by its very nature is affected with a public interest. The public interest is best served, and the most effective patent examination occurs when, at the time an application is being examined, the Office is aware of and evaluates the teachings of all information material to patentability. Each individual associated with the filing and prosecution of a patent application has a duty of candor and good faith in dealing with the Office, which includes a duty to disclose to the Office all information known to that individual to be material to patentability as defined in this section. The duty to disclose information exists with respect to each pending claim until the claim is canceled or withdrawn from consideration, or the application becomes abandoned. Information material to the patentability of a claim that is canceled or withdrawn from consideration need not be submitted if the information is not material to the patentability of any claim remaining under consideration in the application. There is no duty to submit information which is not material to the patentability of any existing claim. The duty to disclose all information known to be material to patentability is deemed to be satisfied if all information known to be material to patentability of any claim issued in a patent was cited by the Office or submitted to the Office in the manner prescribed by §§1.97(b)-(d) and 1.98. However, no patent will be granted on an application in connection with which fraud on the Office was practiced or attempted or the duty of disclosure was violated through bad faith or intentional misconduct. The Office encourages applicants to carefully examine:

(1) prior art cited in search reports of a foreign patent office in a counterpart application, and

(2) the closest information over which individuals associated with the filing or prosecution of a patent application believe any pending claim patentably defines, to make sure that any material information contained therein is disclosed to the Office.

Title 35, U.S. Code § 101

Inventions patentable

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Title 35 U.S. Code § 102

Conditions for patentability; novelty and loss of right to patent

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for patent,

(b) the invention was patented or described in a printed publication in this or foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States, or

(c) he has abandoned the invention, or

(d) the invention was first patented or caused to be patented, or was the subject of an inventor's certificate, by the applicant or his legal representatives or assigns in a foreign country prior to the date of the application for patent in this country on an application for patent or inventor's certificate filed more than twelve months before the filing of the application in the United States, or

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent, or

(f) he did not himself invent the subject matter sought to be patented, or

(g) before the applicant's invention thereof the invention was made in this country by another who had not abandoned, suppressed, or concealed it. In determining priority of invention there shall be considered not only the respective dates of conception and reduction to practice of the invention, but also the reasonable diligence of one who was first to conceive and last to reduce to practice, from a time prior to conception by the other.

Title 35, U.S. Code § 103

Conditions for patentability; non-obvious subject matter

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Title 35, U.S. Code § 112 (in part)

Specification

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Title 35, U.S. Code, § 119

Benefit of earlier filing date in foreign country; right of priority

An application for patent for an invention filed in this country by any person who has, or whose legal representatives or assigns have, previously regularly filed an application for a patent for the same invention in a foreign country which affords similar privileges in the case of applications filed in the United States or to citizens of the United States, shall have the same effect as the same application would have if filed in this country on the date on which the application for patent for the same invention was first filed in such foreign country, if the application in this country is filed within twelve months from the earliest date on which such foreign application was filed; but no patent shall be granted on any application for patent for an invention which had been patented or described in a printed publication in any country more than one year before the date of the actual filing of the application in this country, or which had been in public use or on sale in this country more than one year prior to such filing.

Title 35, U.S. Code, § 120

Benefit or earlier filing date in the United States

An application for patent for an invention disclosed in the manner provided by the first paragraph of section 112 of this title in an application previously filed in the United States, or as provided by section 363 of this title, which is filed by an inventor or inventors named in the previously filed application shall have the same effect, as to such invention, as though filed on the date of the prior application, if filed before the patenting or abandonment of or termination of proceedings on the first application or an application similarly entitled to the benefit of the filing date of the first application and if it contains or is amended to contain a specific reference to the earlier filed application.

Please read carefully before signing the Declaration attached to the accompanying Application.

If you have any questions, please contact Morgan & Finnegan, L.L.P.

Docket No. 3399-4006

COMBINED DECLARATION AND POWER OF ATTORNEY FOR ORIGINAL, DESIGN, NATIONAL STAGE OF PCT, SUPPLEMENTAL, DIVISIONAL, CONTINUATION OR CONTINUATION-IN-PART APPLICATION

As a below named inventor, I hereby declare that:

My residence, post office address and citizenship are as stated below next to my name,

I believe I am the original, first and sole inventor (if only one name is listed below) or an original, first and joint inventor (if plural names are listed below) of the subject matter which is claimed and for which a patent is sought on the invention entitled:

IMPROVEMENTS IN AND RELATING TO DELIVERY CAPSULES

the specification of which

a. ☒ is attached hereto

b. ☐ was filed on as application Serial No. and was amended on . (if applicable).

PCT FILED APPLICATION ENTERING NATIONAL STAGE

c. ☒ was described and claimed in International Application No. PCT/GB00/02616 filed on 7 July 2000 and as amended on . (if any).

I hereby state that I have reviewed and understand the contents of the above-identified specification, including the claims, as amended by any amendment referred to above.

I acknowledge the duty to disclose information which is material to patentability as defined in 37 C.F.R. § 1.56.

I hereby specify the following as the correspondence address to which all communications about this application are to be directed:

SEND CORRESPONDENCE TO:

☒ Bar Code label attached (see right)

☐ Address Shown (see below)

DIRECT TELEPHONE CALLS TO: 212-415-8695
James P. Demers, Ph.D.

☒ I hereby claim foreign priority benefits under Title 35, United States Code § 119 (a)-(d) or under § 365(b) of any foreign application(s) for patent or inventor's certificate or under § 365(a) of any PCT international application(s) designating at least one country other than the U.S. listed below and also have identified below such foreign application(s) for patent or inventor's certificate or such PCT international application(s) filed by me on the same subject matter having a filing date within twelve (12) months before that of the application on which priority is claimed: